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# Surveillance for Human Prion Diseases in Washington State (aka, Precarious Pleated Proteins)

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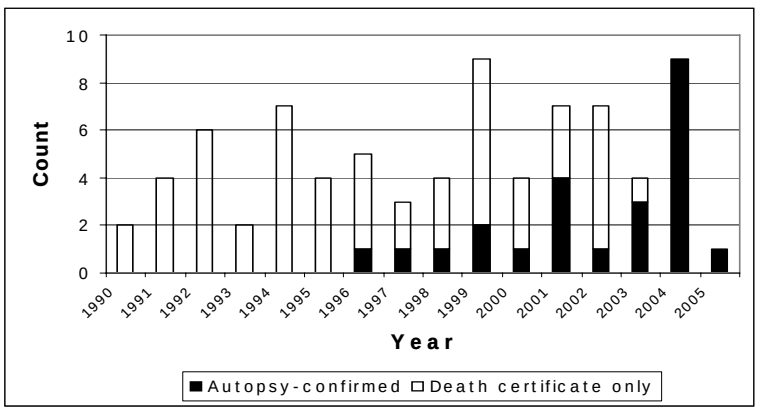
Over the past year, the Washington State Department of Health Communicable Disease Epidemiology Section (DOH CDES) has been working to enhance surveillance for human prion diseases. The goals of this surveillance system are to improve the timeliness and quality of our data by 1) increasing reporting of suspected cases by healthcare providers and 2) increasing autopsy-based confirmation of suspected cases. DOH CDES is currently developing protocols, guidelines and other investigation tools for use by local health departments. From January through June 21, 2006, six cases of autopsy confirmed CJD have been reported in Washington.

Prion diseases, also known as transmissible spongiform encephalopathies (TSEs), are a group of rare, fatal neurodegenerative diseases of animals and humans. The term 'prion' is derived from the phrase "proteinaceous infectious particle". Animal prion diseases include scrapie in sheep, bovine spongiform encephalopathy (BSE, "mad cow") in cattle and chronic wasting disease in deer and elk. The most common human prion disease is Creutzfeldt-Jakob Disease (CJD).

CJD occurs worldwide at an overall rate of one case per million population annually; rates increase to 3 per million population annually in persons over 50 years of age. Since 1990, an average of five cases of CJD are reported on death certificates each year in Washington; less than half have been autopsy-confirmed (Figure).

Figure: Reports of CJD in Washington State, 1990-2005; death certificate data not available for 2005

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Approximately 85% of CJD cases are classified as sporadic (sCJD) and 5-15% of cases are inherited or acquired. Sporadic CJD is caused by a spontaneous change of normal prion proteins into abnormal prion proteins. In 1996, a new form of CJD called variant CJD (vCJD) was identified and has since been reported in nearly 200 persons worldwide, mostly from the United Kingdom (UK) and Europe. Associated with consumption of meat products infected with bovine spongiform encephalopathy (BSE, "mad cow disease"), vCJD has distinctive clinical and pathologic characteristics (Table). Although two cases of vCJD have been reported in the United States (US), epidemiologic investigations concluded that both persons likely acquired the disease while living in the UK. No cases of endemically-acquired vCJD have been identified in the US.

Table: Selected characteristics distinguishing vCJD from sCJD

| Characteristic | vCJD | sCJD |
|---|---|---|
| **Median age at death** | 28 years | 68 years |
| **Median duration of illness** | 13-14 months | 4-5 months |
| **Clinical signs/symptoms** | Prominent psychiatric/behavioral symptoms; painful sensory symptoms; delayed neurologic signs | Progressive dementia; early neurologic signs |

Source: Adapted from Belay E., Schonberger L. Variant Creutzfeldt-Jakob disease and bovine spongiform encephalopathy. Clin Lab Med 2002;22:849

Although clinical characteristics and antemortem tests can suggest a diagnosis of prion disease, examination of brain tissue is required to confirm the diagnosis. Therefore, brain autopsy is encouraged for patients suspected of having a prion disease. Antemortem indicators supporting a diagnosis of CJD may include progressive dementia, myoclonus, periodic sharp waves on EEG and elevated levels of 14-3-3 protein in cerebral spinal fluid (CSF). The 14-3-3 protein is a normal brain protein; detection of elevated levels in CSF may indicate neuronal destruction in the brain with subsequent leakage into CSF. Since other conditions could also cause this to occur, an elevated level of the 14-3-3 protein in CSF is not a specific marker for CJD. The 14-3-3 immunoassay is not a screening test and should be used only when a diagnosis of CJD is strongly suspected. The National Prion Disease Pathology Surveillance Center (NPDPSC) performs 14-3-3 immunoassays and other diagnostic prion disease analyses free of charge.

## Enhancing Surveillance

To improve our understanding of the public health impact of human prion diseases in Washington, state and local public health departments are collaborating with the Centers for Disease Control and Prevention (CDC) and the National Prion Disease Pathology Surveillance Center (NPDPSC) to increase reporting and laboratory confirmation of prion disease cases.

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The goals of surveillance for human prion diseases are to:

- Have a system that can detect the emergence of vCJD in the US,
- Have a system that can detect the emergence of novel prion diseases, including those related to animal prion diseases,
- Prevent iatrogenic transmission of prion diseases, and
- Monitor trends in the epidemiology of disease over time.

## Identifying Suspected Cases of Human Prion Disease

Local health departments and DOH CDES identify persons suspected or confirmed to have human prion disease by:

- Reports from healthcare providers: Prion diseases in humans are notifiable in Washington as "Rare diseases of public health significance" as described in Washington Administrative Code 246-100 and 246-101. Providers are required to report all suspected and confirmed cases to the local health department where the patient resides or to DOH CDES (see Resources below for contact information).
- Reports from the National Prion Disease Pathology and Surveillance Center (NPDPSC): The NPDPSC was established in 1997 in collaboration with the CDC to act as the national reference laboratory for human prion diseases. NPDPSC notifies DOH CDES of all test results for patients that are known to reside or receive healthcare in Washington.
- Review of death certificates: DOH CDES periodically reviews death certificates of Washington decedents to identify prion disease associated deaths.

## Investigating Suspected Cases of Human Prion Disease

Local health departments and/or DOH CDES collect information on suspected cases as follows.

1. Reviewing the clinical presentation: The clinical presentation, age, status (living or deceased) and laboratory tests (i.e., EEG, MRI, 14-3-3 protein) are reviewed to determine whether the patient has/had an illness consistent with CJD (see Table) or another prion disease.

2. Confirming the diagnosis: An autopsy and laboratory examination of brain tissue to confirm the diagnosis of prion disease can be arranged at no cost to the family or provider. Healthcare providers are strongly encouraged to discuss the benefits of autopsy with the patient's family. With permission from the family, postmortem arrangements can be made through the NPDPSC for a brain autopsy. If local resources are unavailable, autopsies can be conducted by a designated neuropathologist at Harborview Medical Center in Seattle under an agreement with the NPDPSC. All expenses including transport of the body, collection of brain tissue, return of the body, specimen shipping and testing of brain tissue are covered by the NPDPSC. Please call the NPDPSC if you need assistance with arranging a brain autopsy (see Resources below). NPDPSC is the national reference laboratory for human prion diseases where advanced neuropathologic and biochemical diagnostics, including histopathology, immunohistochemistry, Western blot and prion gene analysis, are used to identify prion diseases and distinguish the type (e.g., familial vs. sporadic).

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3. Identifying iatrogenically-acquired human prion disease: Although uncommon, human prion disease has been transmitted iatrogenically through human derived pituitary growth hormone, receipt of dura mater and corneal grafts and from contaminated neurosurgical equipment. Any history of such procedures should be noted. If a patient is suspected to have iatrogenically-acquired prion disease, please contact your local health department or DOH CDES (see Resources below).

4. Controlling further spread:

- Neurosurgical procedures: Prions are resistant to routine disinfectants and methods of sterilization used in medical facilities. As a result, neurosurgical or other equipment that has been in contact with nervous tissue of a person suspected to have a prion disease requires special decontamination procedures. Information about recent neurosurgical procedures or invasive EEG monitoring should be collected and reviewed with the facility's infection control program to assure that appropriate control measures are implemented.
- Autopsy and Embalming: World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies should be followed during autopsy and embalming of a patient with suspected or confirmed human prion disease. WHO infection control guidelines can be found at:
  http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf
- Tissue/Organ Donation: Tissues and organs from patients with suspected or confirmed prion disease should not be donated for transplantation or teaching purposes.

## Resources

To support patients' families:

- CJD Foundation operates a national toll-free line [(800) 659-1991] and a Web site:
  http://www.cjdfoundation.org/

To report suspected or confirmed cases of human prion disease:

- Local health departments
  http://www.doh.wa.gov/LHJMap/LHJMap.htm
- Washington State Department of Health, Communicable Disease Epidemiology Section (CDES)
  (206) 418-5500 or toll free at (877) 539-4344

  A DOH CDES Web page on human prion diseases is currently under development, check:
  http://www.doh.wa.gov/EHSPHL/Epidemiology/CD/default.htm

To arrange an autopsy or obtain information about diagnostic testing, specimen collection and shipping of specimens:

- National Prion Disease Pathology Surveillance Center
  (216) 368-0587 or www.cjdsurveillance.com

To obtain additional information about infection control measures related to CJD:

- Centers for Disease Control and Prevention
  http://www.cdc.gov/ncidod/dvrd/cjd/infection_control_cjd.htm
- World Health Organization
  http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf